Drive AB: part of a global collaboration for combatting AMR

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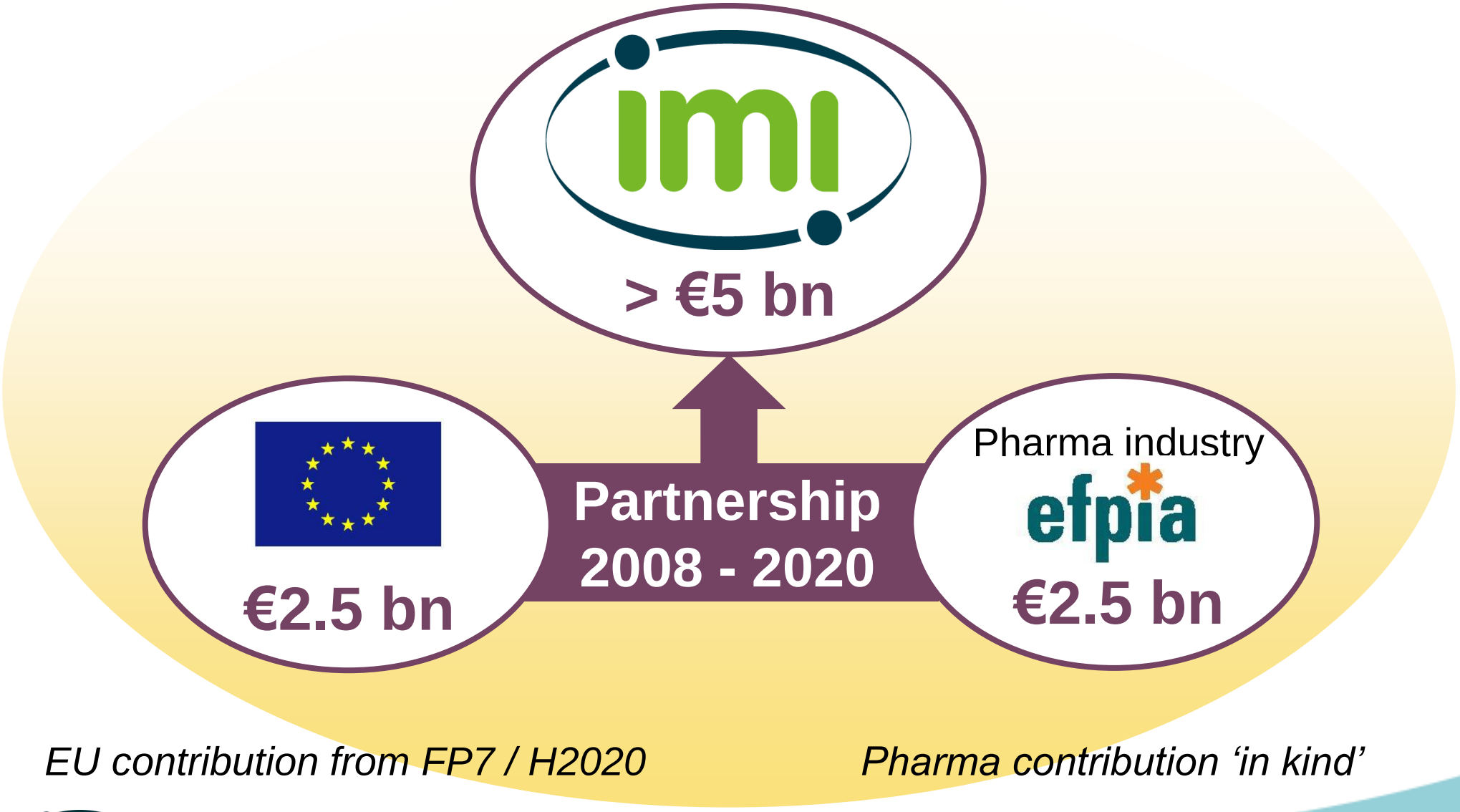
Drive-AB Final Conference: Brussels September 5-6, 2017

IMI – Europe's partnership for health



EU contribution from FP7 / H2020

Pharma contribution 'in kind'

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IMI – Europe's partnership for health

IMI mission

IMI facilitates open collaboration in research to advance the development of, and accelerate patient access to, personalised medicines for the health and wellbeing of all, especially in areas of unmet medical need.

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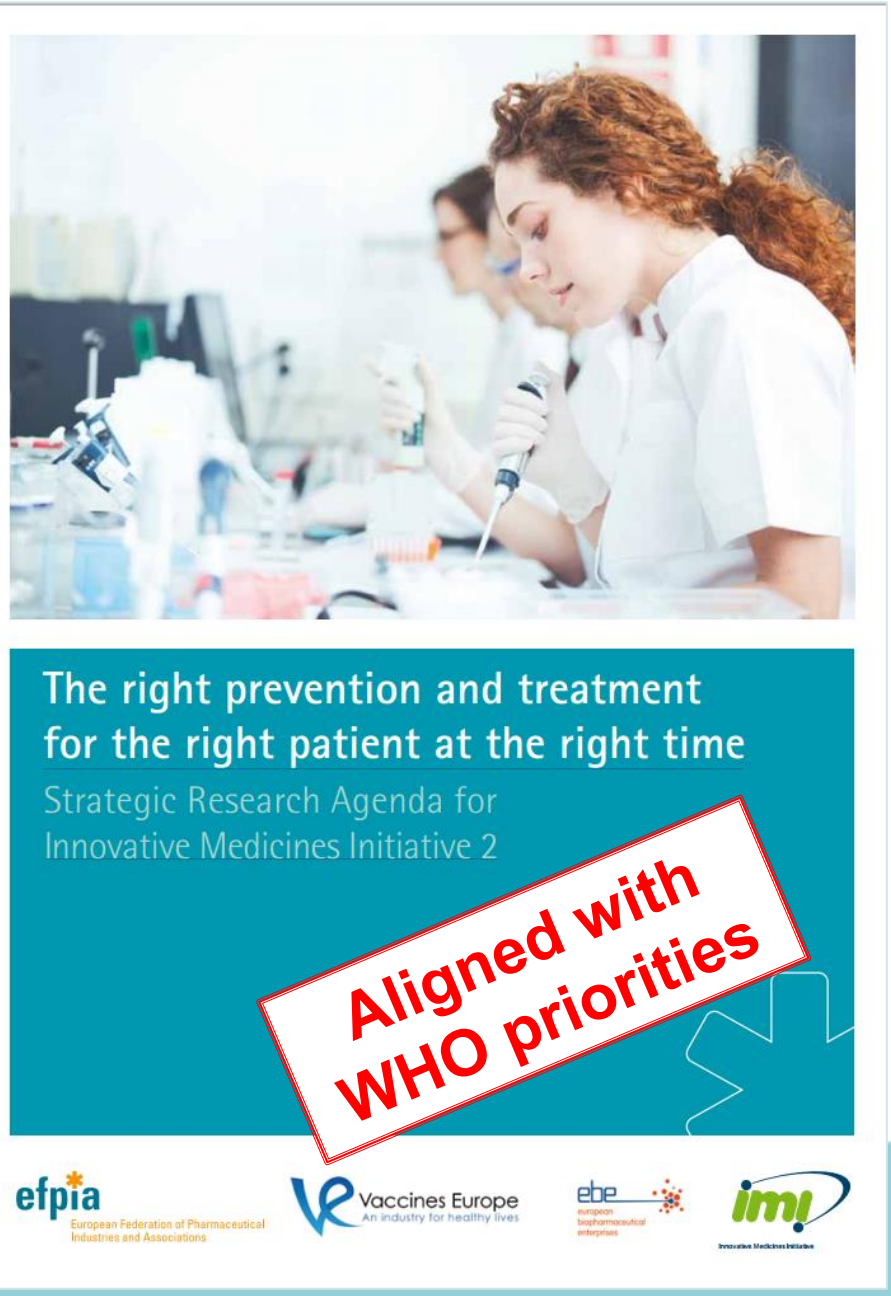
IMI 2 Strategic Research Agenda

- Antimicrobial resistance
- Osteoarthritis
- Cardiovascular diseases
- Diabetes
- Neurodegenerative diseases
- Psychiatric diseases
- Respiratory diseases
- Immune-mediated diseases
- Ageing-associated diseases
- Cancer
- Rare/Orphan Diseases
- Vaccines



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New Drugs for Bad Bugs (ND4BB)

Translocation

Penetration barriers & efflux

ENABLE

Drug discovery engine

Clinical trial networks

COMBACTE-NET

Observational and epidemiology studies
MEDI4893 in *S. aureus infections*
Minocyline in *A. baumannii* infections

DRIVE-AB

New economic models

COMBACTE-CARE

Clinical management & outcomes of patients with CRE
Microbiological analysis and biomarkers
ATM-AVI clinical development

Total budget
>650 million Euro

COMBACTE-MAGNET

Epidemiology network and support
MEDI3902 anti-*P. aruginosa*
First-in-Human trial AIC499

COMBACTE-CDI

Epidemiology, best practices, burden of CDI

iABC Programme

Inhaled Antibiotics in Bronchiectasis and Cystic Fibrosis including Bronchiectasis patient registry (EMBARC)

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ND4BB clinical trial networks

- **CLIN-Net: A clinical investigator network**

Comprises >700 hospitals in 437 cities across 39 countries in Europe

Established certification criteria and GCP training programme

- **LAB-Net: A laboratory surveillance network**

>400 laboratories across Europe

Carrying out assessment of existing laboratory methods, quality assessment system in place, specimens and strains repository

- **STAT-Net: Improvements in trial design**

Statistical support and expertise, dialogue with regulators on novel trial design, novel endpoints,…

- **Epi-Net: Epidemiology support for ND4BB programmes and beyond**

Shared data policy established, definition of specifications for data management and statistical analysis established, web-based platform defined

Automated MDR-HAI surveillance: centers selected and data collection started

Lab sentinel surveillance: protocols and centers approved

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ENABLE – Overall objective

- A ‘drug discovery engine’ for novel mode of action medicines to treat serious systemic Gram-negative infections
- Progression of the most promising Hit-to-Lead and Lead-to-Clinical candidate programmes towards the clinic
- Programmes come from SME’s, academia, or participating EFPIA companies
- Multiple programmes in parallel
- Goal as planned in original call text:
  - 3 ‘lead declaration’
  - 2 ‘candidate declaration’
  - 1 pre-clinical and Phase 1

Budget: EUR 58,900,000 IMI JU, EUR 22,952,360 EFPIA in-kind
Runs from 02/2014 to 01/2020

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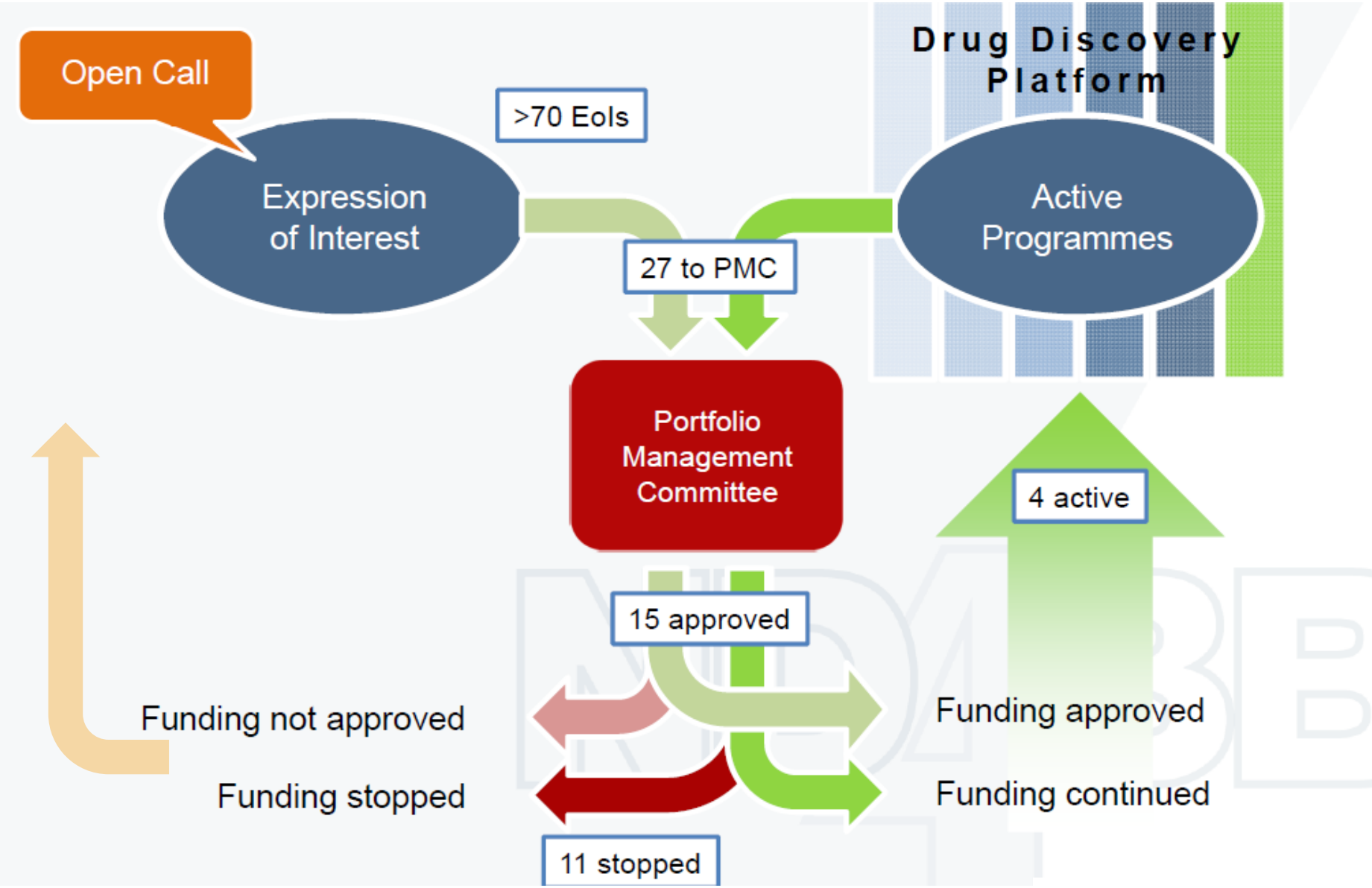
ENABLE model – funding cycle



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Main Achievements

- Highly innovative and effective PPP model for **quick progression and early termination of programmes**
  - Hit owners retain ownership of asset; IP (compound patents and related data) are assigned to hit owner
- Huge effort to attract programmes; outreach to European SME's
- Since project start, **>70 applications through open call process**, 27 different antibiotic drug discovery programmes were reviewed by ENABLE's Portfolio Review Committee; **15 were funded, and 11 terminated again**
- 39 (of 60 total) applications to enter ENABLE with a new development programme came from SMEs; currently, 15 SMEs in ENABLE
- **2 Lead declarations**

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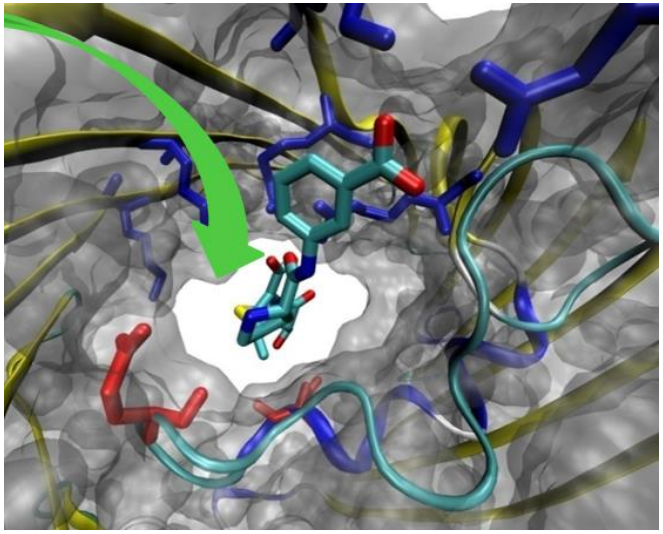
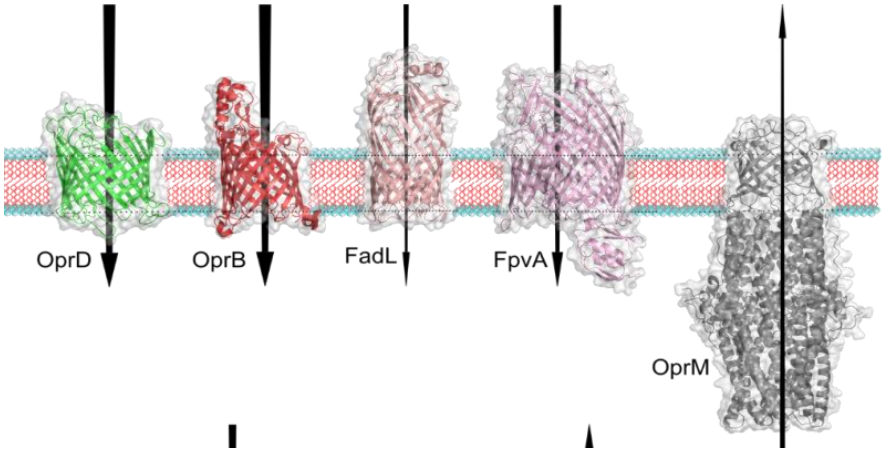
TRANSLOCATION – getting drugs into bugs (& keeping them there)

focus on Gram-negatives





- **>44 new membrane protein structures**: porins, efflux pumps and other transporters
- **Proteomics of the outer cell wall in Pseudomonas**: change in protein levels in different environments & hypotheses about antibiotic and nutrient transport
- **Mass spec and fluorimetric techniques** to quantify intracellular small molecule concentration (including single cells)
- Creation of database (**ND4BB Info Centre**) to gather data from both new antibiotic research projects and abandoned ones.

DRIVE-AB – driving a new economic model for antibiotic R&D

Innovation	Conservation	Access
New antibiotics that address extensively or pan-resistant bacteria	Sustainable use, prevention of excessive use, includes diagnostics, biomarkers, alternative treatment strategies	Access to new antibiotics when needed, excludes extremely high prices

Return on investment de-linked from sales volume

Challenge: Buy-in from all stakeholders: public health, government / payers, clinical societies, academia, industry

DRIVE-AB final conference: September 5/6, 2017, in Brussels

Watch out for final report late 2017!

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Drive AB: A challenging discussion

- General agreement that:
  - Both push and pull mechanisms are needed for successful products to be made available (antimicrobials, diagnostics)
  - Specific conditions will need to be defined which may differ from one geographical region to another
  - Target product profiles and details for sustainable use obligations will need to be developed (by independent bodies) so that it is clear what the need is and what is being made available
- The Drive AB project (like many IMI projects) should provide evidence based research that could be helpful to policy makers involved in this complex area
- This topic has become highly political over the past few years but we should not enter into negotiational types of discussion now, rather, we should be providing as many options as we can based on the evidence generated within the project and elsewhere to help policy makers do their work

Take-home messages from 4 years of ND4BB

- IMI's ND4BB programme catalyzed change and supported the increase of antibiotic drug discovery and development activities
  - high impact on both European SME's and big pharma
- Support at early stage of drug discovery crucial, to ensure the right questions are asked early (quick termination)
- For studies where patient and site selection is difficult, public-private partnership is crucial.
- Also ND4BB is providing the capability in Europe to deliver quality efficacy and safety data to register new antibacterial therapies and support treatment decisions for clinicians.
- New economic model huge on political agenda

ND4BB – where are we heading?

Broadening scope, players, and geographical outreach

Mobilization of diagnostics industry

- The medical, economical, and public health value of diagnostics to address AMR is insufficiently recognized and studied.
- In past 9 months, leading diagnostics companies have started an effort to define a public-private partnership effort under IMI, linking into ND4BB.

Broadening the network

- Transatlantic collaboration clinical trial network: following Januray 2016 workshop in Stockholm, collaboration between CLIN-Net and LAB-Net and one of NIH/NIAID targeted clinical trials on multidrug resistance
- Plans to increase capabilities of current networks for different types of clinical trials with antibiotics

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THANK YOU

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